

endoscopic disease recurrence, according to the Rutgeerts score (graded as ≥ 2). CRP and fCal were measured and the respective performance and usefulness of both surrogate markers with respect to the presence and severity of postoperative endoscopic disease recurrence were assessed by computing correlations, sensitivity, specificity and predictive values at adjusted cutoffs and also tests operating characteristics.

RESULTS: A moderate (≥ 2) and a severe (≥ 3) endoscopic recurrence was observed in 18 and 36 patients, respectively. fCal concentrations differed significantly in patients experiencing evidences for endoscopic recurrence when compared with those in endoscopic remission (mean \pm SEM 484.3 \pm 71 $\mu\text{g/g}$ vs 118 \pm 17 $\mu\text{g/g}$; $p < 0.0001$). The area under the ROC curve (AUROC) to discriminate between patients in endoscopic remission and recurrence was 0.85 for fCal and lower 0.70 for CRP. The best cutoff point for fCal to distinguish between endoscopic remission and recurrence after surgery was 100 $\mu\text{g/g}$, as determined by the ROC curve and its sensitivity, specificity, positive and negative predictive values as well as overall accuracy were 93 %, 57 %, 66 %, 89 % and 74 %, respectively. In our cohort, fCal concentrations lower than 100 $\mu\text{g/g}$ would allow with a high accuracy to avoid colonoscopy in almost 31 % of patients.

CONCLUSION: Measurement of fCal concentrations may be a promising and useful tool for monitoring CD patients after ileocolonic resection. Patients with a concentration of fCal below 100 $\mu\text{g/g}$ are highly likely to be exempt of endoscopic recurrence and therefore fCal measurement in CD patients who had undergone surgery would get some help in making decision for colonoscopy.

Disclosure of Interest: None declared

OP135 PROGNOSTIC VALUE OF COMPLETE REMISSION IN PATIENTS WITH MUCOSAL HEALING IN ULCERATIVE COLITIS

T. Lobatón^{1,2,*}, T. Bessissow¹, G. De Hertogh³, A. Ruiz-Cerulla², S. Vermeire¹, G. Van Assche¹, B. Lemmens¹, R. Bisschops¹, J. Guardiola¹, M. Ferrante¹
¹GASTROENTEROLOGY, LEUVEN UNIVERSITY HOSPITAL, Leuven, Belgium, ²GASTROENTEROLOGY, HOSPITAL UNIVERSITARI DE BELLVITGE, Barcelona, Spain, ³PATHOLOGY, LEUVEN UNIVERSITY HOSPITAL, Leuven, Belgium

Contact E-mail Address: tlobaton@bellvitgehospita.cat

INTRODUCTION: The presence of endoscopic remission (ER) in patients with ulcerative colitis (UC) predicts better outcome with fewer relapses and colectomy rates. However, there is scarce data on the additive prognostic value of histological and biological activity among patients with both clinical and endoscopic remission (complete remission).

AIMS & METHODS: To assess the prognostic value of histological and biological activity in UC patients with clinical and endoscopic remission.

METHODS: Prospective observational study including 77 UC patients in clinical and endoscopic remission from 2 referral centres. Clinical remission was defined as clinical Mayo score < 3 and no blood in the stools. Biological activity was assessed with C-reactive protein haemoglobin and albumin levels, and by leukocyte, and platelet counts. ER was defined as a Mayo endoscopic subscore (MES) of 0-1. Histological activity was assessed according to Geboes score (GS). Histological activity was defined as $GS \geq 3.1$ (neutrophils in the epithelium). Patients were followed up after the endoscopy for 12 months. Clinical relapse (CR) was defined as a clinical Mayo score ≥ 3 . Univariate and multivariate analyses were performed to assess predictors of CR.

RESULTS: Baseline characteristics are summarized in Table 1. During follow up, 21 patients relapsed (9/27 patients with MES grade 1 and 12/50 with MES grade 0; $P = 0.38$), but no colectomies occurred. A $GS \geq 3.1$ was present more often in patients with MES 1 than in patients with MES 0 (48 vs. 14%; $P = 0.002$). CR was more frequent among patients with $GS \geq 3.1$ (43 vs. 20%; $P = 0.034$). After adjusting for endoscopic activity, a $GS \geq 3.1$ remained as an independent risk factor for CR (OR 3.1 (95% CI 1.03-9.09), $P = 0.043$). Patients with basal plasmacytosis presented numerically more CR, but differences were not statistically significant (19 vs. 11%; $P = 0.45$). None of the demographic and biological variables included were predictive for CR (Table 1).

| Baseline characteristics | All patients (n=77) | No relapsers (n=56) | Relapsers (n=21) | P |
|--|---------------------|---------------------|------------------|------|
| Female (%) | 27 (35) | 21 (38) | 6 (28) | 0.47 |
| Median (IQR) age (years) | 51 (41-60) | 51 (42-58) | 50 (37-66) | 0.86 |
| Median (IQR) disease duration (years) | 11 (6-18) | 12 (9-20) | 8 (2-15) | 0.06 |
| Montreal classification(%) | 13/39/25/17/51/32 | 7/29/20/13/52/35 | 4/13/4/19/62/19 | 0.75 |
| E1/E2/E3 | | | | |
| C reactive protein (mg/L): median(IQR) | 1.2 (0.9-2.7) | 1.2 (0.7-2.5) | 1.5 (1-3.6) | 0.09 |
| Hemoglobin (g/dL):median(IQR) | 14.2 (13.2-15.4) | 14.5 (13.2-14.5) | 14.1 (13.3-15.6) | 0.89 |
| WBC (10 ⁹ /L): (IQR) | 5.9 (5-7.9) | 6.0 (4.9-8) | 5.7 (5.1-6.9) | 0.62 |
| Platelets (10 ⁹ /L):median(IQR) | 241 (211-295) | 249 (212-300) | 232 (209-263) | 0.37 |
| Albumin (g/L):median(IQR) | 46 (43-47) | 46 (42-47) | 46 (44-47) | 0.66 |

CONCLUSION: In a prospective cohort, histological activity defined as $GS \geq 3.1$ predicts CR at 1 year among patients with both clinical and endoscopic remission.

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OP136 PROFILING OF SERUM MICRORNA IDENTIFIES NOVEL BIOMARKERS OF FIBROSTENOSING CROHN'S DISEASE

A. Lewis^{1,*}, L.N. Hanna¹, L.A. Rogalski¹, A. Nijhuis¹, S.J. Mehta¹, T. Kumagai¹, P. Biancheri², J.G. Bundy³, C.L. Bishop⁴, A. Di Sabatino⁵, J.O. Lindsay¹, A. Silver¹

¹Centre for Digestive Diseases and National Centre for Bowel Research and Surgical Innovation, Queen Mary's University London, ²Centre for Immunology and Infectious Disease, Barts and The London School of Medicine and Dentistry, ³Department of Surgery and Cancer, Imperial College London, ⁴Centre for Cutaneous Research, Blizard Institute, Barts and The London School of Medicine and Dentistry, London, United Kingdom, ⁵Department of Internal Medicine, S. Matteo Hospital, University of Pavia, Pavia, Italy
Contact E-mail Address: a.lewis@qmul.ac.uk

INTRODUCTION: Fibrostenosing Crohn's disease (CD) leads to stricture formation and bowel obstruction and is the main indication for surgery. A stricturing phenotype is associated with increased healthcare costs, increased morbidity and a worse quality of life. It is often difficult to differentiate inflammation from fibrosis using currently available imaging modalities, and no investigation can predict the future risk of stricture formation. The development of non-invasive biomarkers of fibrostenosing CD would represent a significant clinical advance. MicroRNAs (miRNAs) inhibit protein translation and thereby co-ordinate gene expression networks. MiRNAs are also present in the circulation, where they are resistant to degradation and can act as accurate biomarkers of disease. Our lab has recently demonstrated through targeted assays that the expression of the miR-29 family is reduced in the mucosa overlying stricture and in the serum of patients with a stricturing phenotype (SCD). These data suggest that miRNAs may act as biomarkers of SCD (Nijhuis et al 2014).

AIMS & METHODS: In this study we aimed to explore the potential of serum miRNAs as biomarkers of fibrostenosing CD. Profiling of RNA isolated from serum was performed by qPCR array and used to identify miRNAs associated with SCD (n=6) relative to inflammatory CD (n=11) and healthy controls (n=5). Differentially expressed miRNAs were subsequently validated by single qPCR assay in an independent cohort of CD patients (SCD n=35; inflammatory n=26; and penetrating n=19) and healthy controls (n=10).

RESULTS: A supervised modeling approach indicated that the SCD patients had a unique serum miRNA signature. In this model miR-19a-3p and 19b-3p contributed most strongly to the separation of SCD patients and inflammatory CD patients; changes in miR-29a-3p and 29c-3p also contributed, albeit to a lesser extent. Subsequent qPCR validation in an independent cohort demonstrated a significant reduction in miR-19a-3p and 19b-3p in SCD patients relative to inflammatory and penetrating CD groups (i.e. non-stricturing CD). In this cohort, stepwise linear regression confirmed that the association of the miRNAs with SCD was not affected by confounding factors, e.g. age, smoking status, disease duration etc. Levels of miR-19a-3p and 19b-3p also remained low in SCD patients following surgical resection.

CONCLUSION: We have demonstrated that miR-19a-3p and 19b-3p in serum are novel predictors of fibrostenosing CD. SCD was associated with low levels of miR-19a-3p and 19b-3p. The levels remained low in SCD patients after surgical resection indicating that miR-19a-3p and 19b-3p are markers of an SCD phenotype, and not merely the presence of stricture at the time of sampling. A longitudinal study is required to determine whether a reduction in serum miR-19 levels predates the development of stricture.

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OP137 CD62L (L-SELECTIN) SHEDDING FOR ASSESSMENT OF FUNCTIONAL BLOCKADE OF TNF-ALPHA IN ANTI-TNF TREATED INFLAMMATORY BOWEL DISEASE PATIENTS: CLINICAL FEASIBILITY AND PERSPECTIVES

P. Juillerat^{1,2,*}, P. Andrew², J. Macpherson², E. Slack², J. Cahenzi², F. Seibold^{1,3}, K.D. McCoy², A.J. Macpherson^{1,2}

¹University Clinic for Visceral Surgery and Medicine, Gastroenterology, ²Maurice E Müller Laboratories, Bern University Hospital, ³Gastroenterology, Tiefenau Spital, Bern, Switzerland

Contact E-mail Address: pascal.juillerat@insel.ch

INTRODUCTION: Tumor necrosis factor (TNF) inhibition is central to the therapy of inflammatory bowel diseases (IBD). However, the durability and efficacy of this blockade hasn't been well studied and a better understanding is crucial for the prognosis of long-term treatment and decision making in case of loss of response (LOR) to these costly anti-TNF agents. Besides the presence of antibodies against the drug and serum trough levels additional tests to predict LOR are needed.

AIMS & METHODS: Consecutive IBD Patients receiving anti-TNF therapy (infliximab (IFX) or adalimumab) from Bern University Hospital were identified

and followed prospectively. Patient whole blood was stimulated with a dose-titration of either human TNF or the TLR agonist lipopolysaccharide (LPS) followed by flow cytometry. Median fluorescence intensity of CD62L on the surface of granulocytes was quantified by surface staining with fluorochrome conjugated antibodies against CD33 and CD62L. Logistic curves of these data permit the calculation of EC50 or the concentration of TNF required to induce a 50% shedding of surface CD62L [Patuto *et al*, DDW 2011]. The change in EC50 following the anti-TNF agent infusion, was used to predict the in vivo response to the anti-TNF agent. This predicted response was correlated to the clinical evolution of the patients in order to analyze the ability of this test to identify LOR.

RESULTS: We collected prospective clinical data and 2 blood samples, before and after anti-TNF agent administration, on 33 IBD patients, 25 Crohn's disease and 8 ulcerative colitis patients (45% females) between June 2012 and November 2013. The assay showed a functional blockade (PFR) for 22 patients (17 CD and 5 UC) whereas 11 (8 CD and 3 UC) had no functional response (NR). Selected clinical characteristics between predicted PFR and NR are compared below (Table). Among the 22 Patients with PRF, only 1 patient was a clinical non responders (LOR to IFX), based on clinical prospective evaluation by IBD gastroenterologists (PJ, FS and AJM), and among the 11 predicted NR, 3 had no clinical LOR. Sensitivity of this test was 95% and specificity 73% and AUC adjusted for age and gender was 0.81. During follow up (median 10 months, range 3-15) 8 "hard" outcomes occurred (3 medic. flares, 4 resections and 1 new fistula) 2 in the PFR and 6 in the NR group (25% vs. 75%; $p < 0.01$).

| | Predicted responders (N=22) | Predicted non responders (N=11) | p value |
|-----------------------------------|-----------------------------|---------------------------------|---------|
| Age (years +/-SD) | 34.8 (+/-11) | 31 (+/- 11) | 0.35 |
| Clinical LOR: No/partial/complete | 68%/27%/1% | 27%/27%/46% | 0.01 |
| Perianal | 41% | 12% | 0.15 |
| Dis. Dur. start IFX (years +/-SD) | 6.9 (+/- 6) | 3.6 (+/- 4) | 0.07 |
| Interval reduction needed | 23% | 73% | < 0.01 |
| Smokers | 33% | 36% | 0.684 |

CONCLUSION: CD62L (L-Selectin) shedding is the first validated test of functional blockade of TNF alpha in anti-TNF treated IBD patients and will be a useful tool to guide medical decision on the use of anti-TNF agents. Prospective comparative studies with antibodies against the drug and trough levels are ongoing.

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OP138 THE NEW FECAL MARKER MATRIX METALLOPROTEASE-9 IS MORE SENSITIVE FOR DIAGNOSING ULCERATIVE COLITIS AND POUCHITIS AND FOR DIFFERENTIATING THEM FROM CROHN'S DISEASE THAN FECAL CALPROTECTIN

K. Farkas^{1,*}, Z. Saródi¹, A. Bálint¹, I. Földesi¹, G. Lázár², Z. Simonka², L. Tiszlavicz³, M. Szűcs⁴, T. Nyári⁴, F. Nagy¹, S. Szepes¹, R. Bor¹, A. Annaházi¹, R. Róka¹, T. Wittmann¹, T. Molnár¹

¹First Department of Medicine, ²Department of Surgery, ³Department of Pathology, ⁴Department of Medical Physics and Informatics, University of Szeged, Szeged, Hungary

Contact E-mail Address: farkas.klaudia@gmail.com

INTRODUCTION: Inflammatory biomarkers that correlate with enteric inflammation would be beneficial for monitoring the course of disease and targeting treatment in patients with inflammatory bowel disease (IBD). Only limited data are available about the diagnostic accuracy of fecal matrix metalloprotease (MMP)-9 in IBD.

AIMS & METHODS: The aims of our prospective study was to assess the diagnostic accuracy of fecal MMP-9 in patients with active Crohn's disease (CD), ulcerative colitis (UC) and pouchitis assessed by clinical, endoscopic and histological scores and to compare the diagnostic accuracy of fecal MMP-9 and fecal calprotectin (CP) in IBD. Stool and blood samples were collected in 50 CD, 54 UC and 34 ileal pouch-anal anastomosis patients before control endoscopy. Biopsies were taken for histology. The activities of CD, UC and pouchitis were defined with the use of clinical, endoscopic and histological activity scores (CDAI, partial Mayo score, PDAI, SES-CD, Mayo endoscopic subscore, D'Haens and Riley score). Fecal CP and MMP-9 levels were quantified by use of enzyme-linked immunosorbent assay.

RESULTS: Active CD, UC and pouchitis was detected in 38%, 54% and 29% of the patients. Significant correlation was revealed between fecal CP and the clinical activities of CD and UC, and between fecal CP and the endoscopic activity of UC and pouchitis. No correlation was found between fecal CP and the other examined activity scores in CD, UC and pouchitis. Fecal MMP-9 did not correlate with any of the activity indices of CD, however strong association was shown between fecal MMP-9 and clinical, endoscopic and histological activities of both UC and pouchitis.

CONCLUSION: This is the first study assessing the diagnostic accuracy of MMP-9 in different types of IBD. Our results showed that fecal MMP-9 has an exclusively high specificity in the detection of active UC and pouchitis. These non-invasive methods help assessing intestinal inflammation and also differentiating between CD and UC.

Disclosure of Interest: None declared

OP139 FC GAMMA RECEPTOR MUTATIONS FOR PREDICTION OF SUSTAINED CLINICAL REMISSION AFTER INFLIXIMAB DISCONTINUATION IN CROHN'S DISEASE PATIENTS

K. Papamichail^{1,*}, M. Arias¹, M. Ferrante¹, V. Ballet¹, K. Claes¹, W.J. Wollants¹, G. Van Assche¹, P.J. Rutgeerts¹, S. Vermeire¹

¹KU Leuven, Department of Clinical and Experimental Medicine and University Hospitals Leuven, Department of Gastroenterology, Leuven, Belgium
Contact E-mail Address: konstantinos.papamichail@med.kuleuven.be

INTRODUCTION: Genetic markers, as compared to serologic markers, could theoretically be superior for predicting inflammatory bowel disease (IBD) outcomes as genes are not affected by disease activity and are stable over time. Genetic polymorphisms of Fc gamma receptors (FcγR) may affect the efficacy of immunoglobulin (Ig)-based therapies by influencing the affinity of Ig to the receptors. We therefore hypothesized that these could facilitate prediction of sustained remission after anti-TNF discontinuation in IBD.

AIMS & METHODS: We aimed to investigate if polymorphisms in the *FcγRIIIa*, *FcγRIIIa* and *FcγRIIIb* genes are predictive of sustained clinical remission (SCR) after infliximab (IFX) cessation for clinical remission in Crohn's disease (CD) patients. In this single-center retrospective study, 100 CD patients who discontinued IFX for clinical remission (luminal CD, n=57) were identified from an electronic database. The majority of patients (n=84) continued on immunomodulators. SCR was defined as maintained disease remission without the need to re-introduce medical therapy (biologicals, corticosteroids, thiopurines or methotrexate) or surgery until the end of follow up. The functional polymorphisms 131H/R in *FcγRIIIa* (n=84), 158V/F in *FcγRIIIa* (n=91) and NA1/NA2 in *FcγRIIIb* (n=87) were analyzed by PCR-RFLP / TaqMan.

RESULTS: With a median follow up of 9.7 (IQR 8-11.5) years, 52/100 patients had SCR. Univariate (Log-Rank) analysis revealed no significant association of the investigated polymorphisms with either SCR or relapse after IFX discontinuation for clinical remission. Nevertheless, individual analysis of patients with luminal CD interestingly showed that NA2/NA2 homozygosity in *FcγRIIIb* was associated with increased risk for relapse (HR:2.4, 95%CI:1.1-5.3, p=0.021). Multiple COX regression analysis identified NA2/NA2 homozygosity as an independent variable predicting relapse after IFX cessation (HR:2.3, 95%CI:1.03-5.1, p=0.043).

CONCLUSION: We identified that *FcγRIIIb* NA2/NA2 homozygosity is an independent factor predicting relapse in patients with luminal CD who discontinue IFX for clinical remission. The lack of NA1 variant, which shows a higher affinity for IgG1 and probably leads to a more efficient downstream effects (antibody-dependent cellular cytotoxicity), may therefore predispose to relapse after IFX cessation in patients with luminal CD. Of note, NA1/NA1 homozygosity was previously found to be associated with higher biological response to IFX in IBD patients.

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OP140 PHARMACOLOGICAL INTERVENTION BASED ON FECAL CALPROTECTIN LEVELS IN PATIENTS WITH ULCERATIVE COLITIS AT HIGH RISK OF A RELAPSE: A PROSPECTIVE, RANDOMIZED, CONTROLLED STUDY

A. Låsson^{1,*}, L. Öhman^{2,3}, S. Per-Ove³, S. Isaksson^{2,3}, O. Überbacher⁴, K.-A. Ung⁵, H. Strid³

¹Department of Internal Medicine, Södra Älvsborgs Hospital, Borås, ²Department of Biomedicine, Sahlgrenska Academy, ³Department of Internal Medicine, Sahlgrenska University Hospital, Gothenburg, ⁴Department of Internal Medicine, Hallands Hospital, Varberg, ⁵Department of Internal Medicine, Skaraborgs Hospital, Skövde, Sweden

Contact E-mail Address: anders.lasson@vgregion.se

INTRODUCTION: Pharmacological treatment of ulcerative colitis (UC) is traditionally divided into treatment of active disease and treatment to maintain remission. Recently, targeted therapy for patients at increased risk of a flare, using biomarkers to detect subclinical disease activity, has been proposed. The objective of this study was to assess if fecal calprotectin (FC), as a marker for inflammatory activity, can be used to guide medical intervention, to maintain remission in patients with UC.

AIMS & METHODS: In this open-label, prospective, controlled study, 91 adult patients with UC in clinical remission, and under treatment with an oral 5-ASA agent, were randomized to either an intervention group (n=51) or a control group (n=40). All patients had at least one flare within one year prior to the